AMENDMENTS TO THE CLAIMS

1. (cancelled)

2. (currently amended) A method of claim 19 ~~the compound of claim 1~~ wherein Z^1 and Z^2 are each R^7-aryl.

3. (currently amended) A ~~compound~~ method of claim 2 wherein Z^1 and Z^2 are each R^7-phenyl.

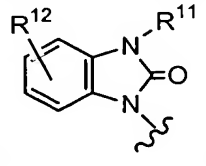
4. (currently amended) A ~~compound~~ method of claim 3 wherein R^7 is selected from the group consisting of $(C_1$-$C_6)$alkyl and halo.

5. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein R^1, R^2, R^3 and R^4 are each hydrogen.

6. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein R^1 and R^3 are each hydrogen and R^2 and R^4 are an alkylene bridge of 2 or 3 carbons.

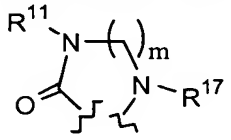
7. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein X^1 is R^7-aryl and and X^2 is OH or [-NC(O)R^{28}] –NC(O)R^{21}.

8. (currently amended) A method ~~compound~~ of claim 7 wherein X^1 is R^7-phenyl.

9. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein X^1 is  and X^2 is hydrogen.

10. (currently amended) A method ~~compound~~ of claim 9 wherein R^{12} is hydrogen and R^{11} is $(C_1\text{-}C_6)$alkyl, -$(C_1\text{-}C_6)$ alkyl$(C_3\text{-}C_{12})$cycloalkyl, -$(C_1\text{-}C_6)$alkyl-OR^{19} or -$(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$.

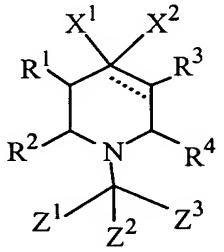
11. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein X^1 and X^2 together form the spirocyclic group



12. (currently amended) A method ~~compound~~ of claim 11 wherein m is 1, R^{17} is phenyl and R^{16} is -$(C_1\text{-}C_6)$alkyl-OR^{19} or -$(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$.

13 to 18. (cancelled)

19. (new) A method of treating cough comprising administering a combination of an effective amount of an ORL-1 agonist of the formula



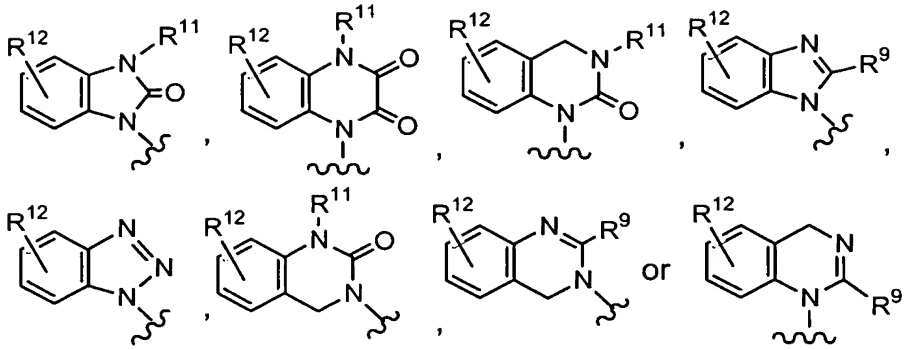
or a pharmaceutically acceptable salt or solvate thereof, wherein:

the dotted line represents an optional double bond;

X^1 is R^5-$(C_1\text{-}C_{12})$alkyl, R^6-$(C_3\text{-}C_{12})$cycloalkyl, R^7-aryl, R^8-heteroaryl or R^{10}-$(C_3\text{-}C_7)$heterocycloalkyl;

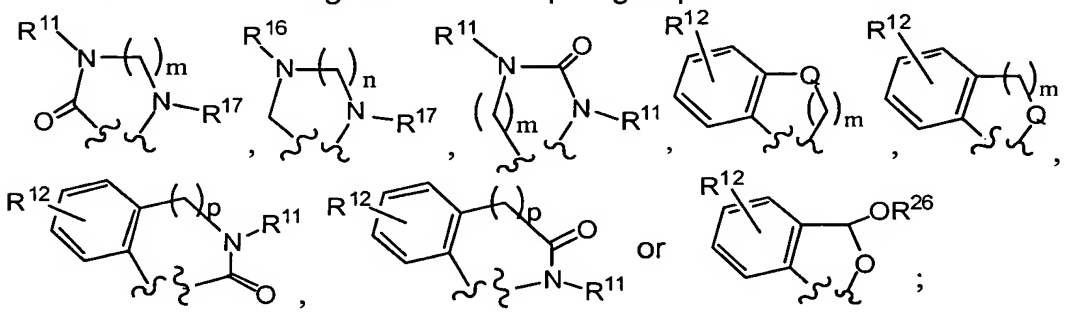
X^2 is -CHO, -CN, -$NHC(=NR^{26})NHR^{26}$, -$CH(=NOR^{26})$, -$NHOR^{26}$, R^7-aryl, R^7-aryl$(C_1\text{-}C_6)$alkyl, R^7-aryl$(C_1\text{-}C_6)$alkenyl, R^7-aryl$(C_1\text{-}C_6)$-alkynyl, -$(CH_2)_vOR^{13}$, -$(CH_2)_vCOOR^{27}$, -$(CH_2)_vCONR^{14}R^{15}$, -$(CH_2)_vNR^{21}R^{22}$ or -$(CH_2)_vNHC(O)R^{21}$, wherein v is zero, 1, 2 or 3 and wherein q is 1 to 3 and a is 1 or 2;

or X^1 is



and X^2 is hydrogen;

or X^1 and X^2 together form a spiro group of the formula



m is 1 or 2;

n is 1, 2 or 3, provided that when n is 1, one of R^{16} and R^{17} is $-C(O)R^{28}$;

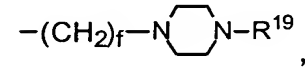
p is 0 or 1;

Q is $-CH_2-$, -O-, -S-, -SO-, $-SO_2-$ or $-NR^{17}-$;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of hydrogen and (C_1-C_6)alkyl, or (R^1 and R^4) or (R^2 and R^3) or (R^1 and R^3) or (R^2 and R^4) together can form an alkylene bridge of 1 to 3 carbon atoms;

R^5 is 1 to 3 substituents independently selected from the group consisting of H, R^7-aryl, R^6-(C_3-C_{12})cycloalkyl, R^8-heteroaryl, R^{10}-(C_3-C_7)heterocycloalkyl, $-NR^{19}R^{20}$, $-OR^{13}$ and $-S(O)_{0-2}R^{13}$;

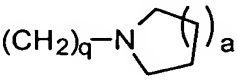
R^6 is 1 to 3 substituents independently selected from the group consisting of H, (C_1-C_6)alkyl, R^7-aryl, $-NR^{19}R^{20}$, $-OR^{13}$ and $-SR^{13}$;

R^7 is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, $(C_1\text{-}C_6)$alkyl, R^{25}-aryl, $(C_3\text{-}C_{12})$cycloalkyl, -CN, $-CF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-OCF_3$, $-NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-NHSO_2R^{19}$, $-SO_2N(R^{26})_2$, $-SO_2R^{19}$, $-SOR^{19}$, $-SR^{19}$, $-NO_2$, $-CONR^{19}R^{20}$, $-NR^{20}COR^{19}$, $-COR^{19}$, $-COCF_3$, $-OCOR^{19}$, $-OCO_2R^{19}$, $-COOR^{19}$, $-(C_1\text{-}C_6)$alkyl-$NHCOOC(CH_3)_3$, $-(C_1\text{-}C_6)$alkyl-$NHCOCF_3$, $-(C_1\text{-}C_6)$alkyl-$NHSO_2$-$(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl-NHCONH-$(C_1\text{-}C_6)$-alkyl or  , wherein f is 0 to 6; or R^7 substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

R^8 is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, $(C_1\text{-}C_6)$alkyl, R^{25}-aryl, $(C_3\text{-}C_{12})$cycloalkyl, -CN, $-CF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-OCF_3$, $-NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-NHSO_2R^{19}$, $-SO_2N(R^{26})_2$, $-NO_2$, $-CONR^{19}R^{20}$, $-NR^{20}COR^{19}$, $-COR^{19}$, $-OCOR^{19}$, $-OCO_2R^{19}$ and $-COOR^{19}$;

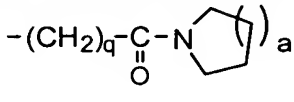
R^9 is hydrogen, $(C_1\text{-}C_6)$alkyl, halo, $-OR^{19}$, $-NR^{19}R^{20}$, -NHCN, $-SR^{19}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

R^{10} is H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

R^{11} is independently selected from the group consisting of H, R^5-$(C_1\text{-}C_6)$alkyl, R^6-$(C_3\text{-}C_{12})$cycloalkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$ and  , wherein q and a are as defined above;

R^{12} is H, $(C_1\text{-}C_6)$alkyl, halo, $-NO_2$, $-CF_3$, $-OCF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

R^{13} is H, $(C_1\text{-}C_6)$alkyl, R^7-aryl, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-SR^{19};

R^{14} and R^{15} are independently selected from the group consisting of H, R^5-(C_1-C_6)alkyl, R^7-aryl and  , wherein q and a are as defined above;

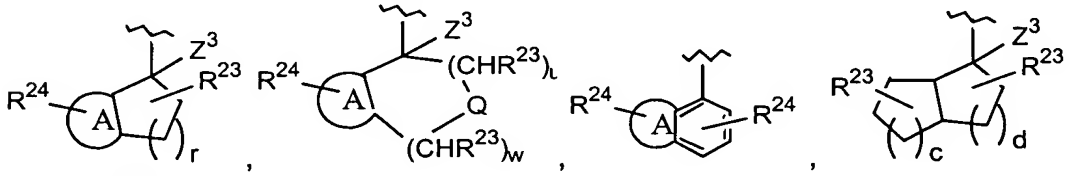
R^{16} and R^{17} are independently selected from the group consisting of hydrogen, R^5-(C_1-C_6)alkyl, R^7-aryl, (C_3-C_{12})cycloalkyl, R^8-heteroaryl, R^8-heteroaryl(C_1-C_6)alkyl, -C(O)R^{28}, -(C_1-C_6)alkyl(C_3-C_7)-heterocycloalkyl, -(C_1-C_6)alkyl-OR^{19} and -(C_1-C_6)alkyl-SR^{19};

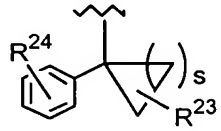
R^{19} and R^{20} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{12})cycloalkyl, aryl and aryl(C_1-C_6)alkyl;

R^{21} and R^{22} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{12})cycloalkyl, (C_3-C_{12})cycloalkyl(C_1-C_6)alkyl, (C_3-C_7)heterocycloalkyl, -(C_1-C_6)alkyl(C_3-C_7)-heterocycloalkyl, R^7-aryl, R^7-aryl(C_1-C_6)alkyl, R^8-heteroaryl(C_1-C_{12})alkyl, -(C_1-C_6)alkyl-OR^{19}, -(C_1-C_6)alkyl-N$R^{19}R^{20}$, -(C_1-C_6)alkyl-SR^{19}, -(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl-O-(C_1-C_6)alkyl and -(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl;

R^{18} is hydrogen or (C_1-C_6)alkyl;

Z^1 is R^5-(C_1-C_{12})alkyl, R^7-aryl, R^8-heteroaryl, R^6-(C_3-C_{12})cyclo-alkyl, R^{10}-(C_3-C_7)heterocycloalkyl, -CO_2(C_1-C_6)alkyl, CN or -C(O)N$R^{19}R^{20}$; Z^2 is hydrogen or Z^1; Z^3 is hydrogen or (C_1-C_6)alkyl; or Z^1, Z^2 and Z^3, together with the carbon to which they are attached, form the group



or  , wherein r is 0 to 3; w and u are each 0-3, provided that the sum of w and u is 1-3; c and d are independently 1 or 2; s is 1 to 5; and ring

A is a fused R^7-phenyl or R^8-heteroaryl ring;

R^{23} is 1 to 3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-NR^{19}R^{20}$ and $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

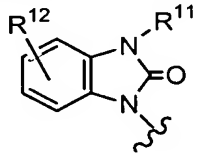
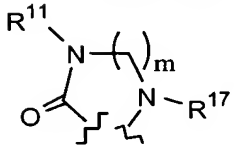
R^{24} is 1 to 3 substituents independently selected from the group consisting of R^{23}, $-CF_3$, $-OCF_3$, NO_2 or halo, or R^{24} substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

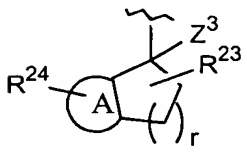
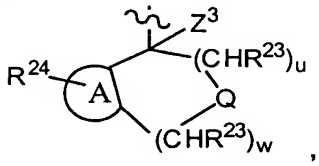
R^{25} is 1-3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and halo;

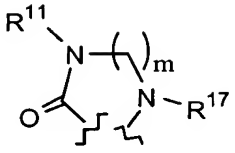
R^{26} is independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl and $R^{25}\text{-}C_6H_4\text{-}CH_2$-;

R^{27} is H, $(C_1\text{-}C_6)$alkyl, R^7-aryl$(C_1\text{-}C_6)$alkyl, or $(C_3\text{-}C_{12})$cycloalkyl;

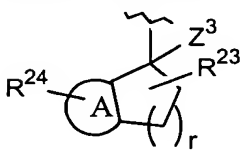
R^{28} is $(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, R^7-aryl, R^7-aryl-$(C_1\text{-}C_6)$alkyl, R^8-heteroaryl, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-OR^{19} or $-(C_1\text{-}C_6)$alkyl-SR^{19};

provided that when X^1 is  or X^1 and X^2 together are  and Z^1 is R^7-phenyl, Z^2 is not hydrogen or $(C_1\text{-}C_3)$alkyl;

provided that when Z^1, Z^2 and Z^3, together with the carbon to which they are attached, form  or  , and X^1 and X^2 together are


, R^{11} is not H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$hydroxyalkyl;

provided that when R^2 and R^4 form an alkylene bridge, Z^1, Z^2 and Z^3, together with the carbon to which they are attached, are not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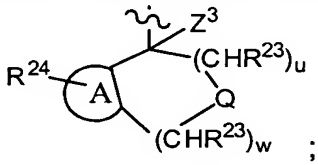
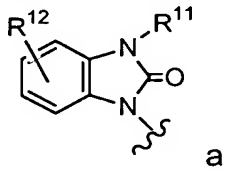
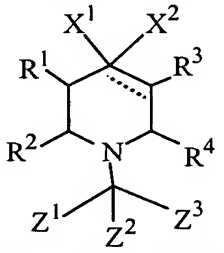

; and


provided that when X^1 is and Z^1 is R^6-$(C_3\text{-}C_{12})$-cycloalkyl, Z^2 is not H;

and an effective amount of second agent for treating cough, allergy or asthma symptoms selected from the group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, H_3 inhibitors, ß-adrenergic receptor agonists, xanthine derivatives, α–adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, NK_1, NK_2 and NK_3 tachykinin receptor antagonists, and $GABA_B$ agonists.

20. (new) A pharmaceutical composition comprising: a therapeutically effective amount of a nociceptin receptor ORL-1 agonist of the formula

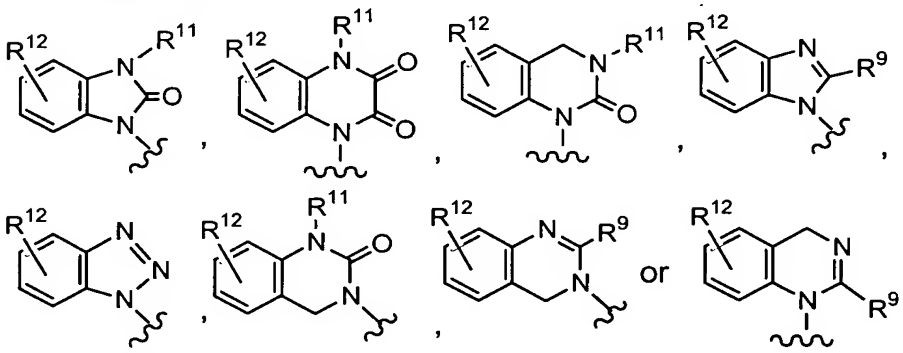

or a pharmaceutically acceptable salt or solvate thereof, wherein:

the dotted line represents an optional double bond;

X^1 is R^5-(C_1-C_{12})alkyl, R^6-(C_3-C_{12})cycloalkyl, R^7-aryl, R^8-heteroaryl or R^{10}-(C_3-C_7)heterocycloalkyl;

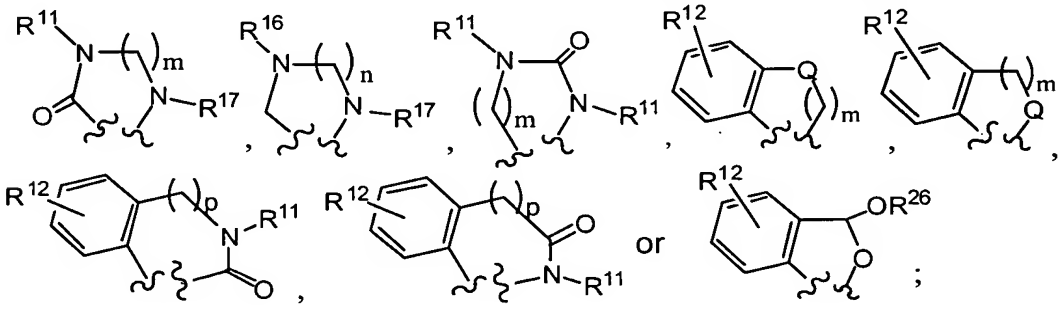
X^2 is -CHO, -CN, -NHC(=NR^{26})NHR^{26}, -CH(=NOR^{26}), -$NHOR^{26}$, R^7-aryl, R^7-aryl(C_1-C_6)alkyl, R^7-aryl(C_1-C_6)alkenyl, R^7-aryl(C_1-C_6)-alkynyl, -$(CH_2)_vOR^{13}$, -$(CH_2)_vCOOR^{27}$, -$(CH_2)_vCONR^{14}R^{15}$, -$(CH_2)_vNR^{21}R^{22}$ or -$(CH_2)_vNHC(O)R^{21}$, wherein v is zero, 1, 2 or 3 and wherein q is 1 to 3 and a is 1 or 2;

or X^1 is



and X^2 is hydrogen;

or X^1 and X^2 together form a spiro group of the formula



m is 1 or 2;

n is 1, 2 or 3, provided that when n is 1, one of R^{16} and R^{17} is -$C(O)R^{28}$;

p is 0 or 1;

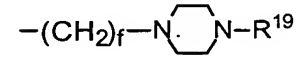
Q is -CH_2-, -O-, -S-, -SO-, -SO_2- or -NR^{17}-;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of hydrogen and (C_1-C_6)alkyl, or (R^1 and R^4) or (R^2 and R^3) or

(R^1 and R^3) or (R^2 and R^4) together can form an alkylene bridge of 1 to 3 carbon atoms;

R^5 is 1 to 3 substituents independently selected from the group consisting of H, R^7-aryl, R^6-(C_3-C_{12})cycloalkyl, R^8-heteroaryl, R^{10}-(C_3-C_7)heterocycloalkyl, -$NR^{19}R^{20}$, -OR^{13} and -$S(O)_{0-2}R^{13}$;

R^6 is 1 to 3 substituents independently selected from the group consisting of H, (C_1-C_6)alkyl, R^7-aryl, -$NR^{19}R^{20}$, -OR^{13} and -SR^{13};

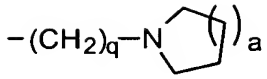
R^7 is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, (C_1-C_6)alkyl, R^{25}-aryl, (C_3-C_{12})cycloalkyl, -CN, -CF_3, -OR^{19}, -(C_1-C_6)alkyl-OR^{19}, -OCF_3, -$NR^{19}R^{20}$, -(C_1-C_6)alkyl-$NR^{19}R^{20}$, -$NHSO_2R^{19}$, -$SO_2N(R^{26})_2$, -SO_2R^{19}, -SOR^{19}, -SR^{19}, -NO_2, -$CONR^{19}R^{20}$, -$NR^{20}COR^{19}$, -COR^{19}, -$COCF_3$, -$OCOR^{19}$, -OCO_2R^{19}, -$COOR^{19}$, -(C_1-C_6)alkyl-$NHCOOC(CH_3)_3$, -(C_1-C_6)alkyl-$NHCOCF_3$, -(C_1-C_6)alkyl-$NHSO_2$-(C_1-C_6)alkyl, -(C_1-C_6)alkyl-NHCONH-(C_1-C_6)-alkyl or  , wherein f is 0 to 6; or R^7 substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

R^8 is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, (C_1-C_6)alkyl, R^{25}-aryl, (C_3-C_{12})cycloalkyl, -CN, -CF_3, -OR^{19}, -(C_1-C_6)alkyl-OR^{19}, -OCF_3, -$NR^{19}R^{20}$, -(C_1-C_6)alkyl-$NR^{19}R^{20}$, -$NHSO_2R^{19}$, -$SO_2N(R^{26})_2$, -NO_2, -$CONR^{19}R^{20}$, -$NR^{20}COR^{19}$, -COR^{19}, -$OCOR^{19}$, -OCO_2R^{19} and -$COOR^{19}$;

R^9 is hydrogen, (C_1-C_6)alkyl, halo, -OR^{19}, -$NR^{19}R^{20}$, -NHCN, -SR^{19} or -(C_1-C_6)alkyl-$NR^{19}R^{20}$;

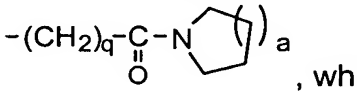
R^{10} is H, (C_1-C_6)alkyl, -OR^{19}, -(C_1-C_6)alkyl-OR^{19}, -$NR^{19}R^{20}$ or -(C_1-C_6)alkyl-$NR^{19}R^{20}$;

R^{11} is independently selected from the group consisting of H, R^5-(C_1-C_6)alkyl, R^6-(C_3-C_{12})cycloalkyl, -(C_1-C_6)alkyl(C_3-C_{12})cycloalkyl,

-(C_1-C_6)alkyl-OR^{19}, -(C_1-C_6)alkyl-$NR^{19}R^{20}$ and  , wherein q and a are as defined above;

R^{12} is H, (C_1-C_6)alkyl, halo, -NO_2, -CF_3, -OCF_3, -OR^{19}, -(C_1-C_6)alkyl-OR^{19}, -$NR^{19}R^{20}$ or -(C_1-C_6)alkyl-$NR^{19}R^{20}$;

R^{13} is H, (C_1-C_6)alkyl, R^7-aryl, -(C_1-C_6)alkyl-OR^{19}, -(C_1-C_6)alkyl-$NR^{19}R^{20}$ or -(C_1-C_6)alkyl-SR^{19};

R^{14} and R^{15} are independently selected from the group consisting of H, R^5-(C_1-C_6)alkyl, R^7-aryl and  , wherein q and a are as defined above;

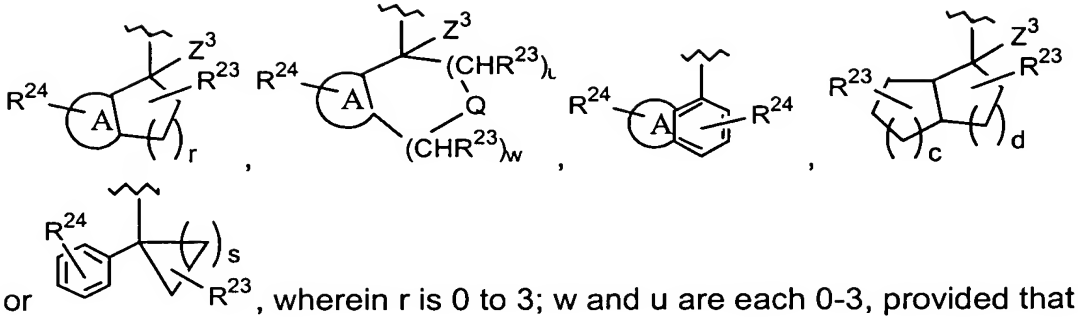
R^{16} and R^{17} are independently selected from the group consisting of hydrogen, R^5-(C_1-C_6)alkyl, R^7-aryl, (C_3-C_{12})cycloalkyl, R^8-heteroaryl, R^8-heteroaryl(C_1-C_6)alkyl, -$C(O)R^{28}$, -(C_1-C_6)alkyl(C_3-C_7)-heterocycloalkyl, -(C_1-C_6)alkyl-OR^{19} and -(C_1-C_6)alkyl-SR^{19};

R^{19} and R^{20} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{12})cycloalkyl, aryl and aryl(C_1-C_6)alkyl;

R^{21} and R^{22} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{12})cycloalkyl, (C_3-C_{12})cycloalkyl(C_1-C_6)alkyl, (C_3-C_7)heterocycloalkyl, -(C_1-C_6)alkyl(C_3-C_7)-heterocycloalkyl, R^7-aryl, R^7-aryl(C_1-C_6)alkyl, R^8-heteroaryl(C_1-C_{12})alkyl, -(C_1-C_6)alkyl-OR^{19}, -(C_1-C_6)alkyl-$NR^{19}R^{20}$, -(C_1-C_6)alkyl-SR^{19}, -(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl-O-(C_1-C_6)alkyl and -(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl-NR^{18}-(C_1-C_6)alkyl;

R^{18} is hydrogen or (C_1-C_6)alkyl;

Z^1 is R^5-(C_1-C_{12})alkyl, R^7-aryl, R^8-heteroaryl, R^6-(C_3-C_{12})cyclo-alkyl, R^{10}-(C_3-C_7)heterocycloalkyl, -CO_2(C_1-C_6)alkyl, CN or -$C(O)NR^{19}R^{20}$; Z^2 is hydrogen or Z^1; Z^3 is hydrogen or (C_1-C_6)alkyl; or Z^1, Z^2 and Z^3, together with the carbon to which they are attached, form the group



or , wherein r is 0 to 3; w and u are each 0-3, provided that the sum of w and u is 1-3; c and d are independently 1 or 2; s is 1 to 5; and ring A is a fused R^7-phenyl or R^8-heteroaryl ring;

R^{23} is 1 to 3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-OR^{19}, $-NR^{19}R^{20}$ and $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

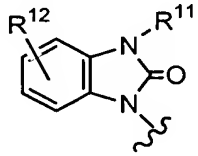
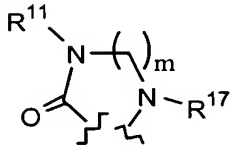
R^{24} is 1 to 3 substituents independently selected from the group consisting of R^{23}, $-CF_3$, $-OCF_3$, NO_2 or halo, or R^{24} substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

R^{25} is 1-3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and halo;

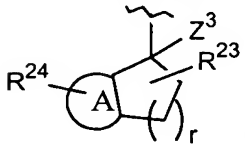
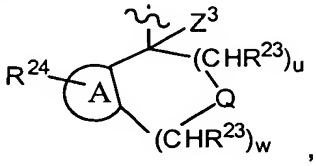
R^{26} is independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl and $R^{25}\text{-}C_6H_4\text{-}CH_2$-;

R^{27} is H, $(C_1\text{-}C_6)$alkyl, R^7-aryl$(C_1\text{-}C_6)$alkyl, or $(C_3\text{-}C_{12})$cycloalkyl;

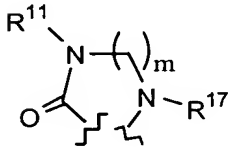
R^{28} is $(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, R^7-aryl, R^7-aryl-$(C_1\text{-}C_6)$alkyl, R^8-heteroaryl, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-OR^{19} or $-(C_1\text{-}C_6)$alkyl-SR^{19};

provided that when X^1 is  or X^1 and X^2 together are  and Z^1 is R^7-phenyl, Z^2 is not hydrogen or $(C_1\text{-}C_3)$alkyl;

provided that when Z^1, Z^2 and Z^3, together with the carbon to which they are attached, form

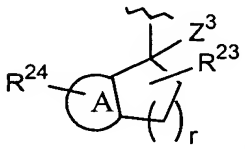
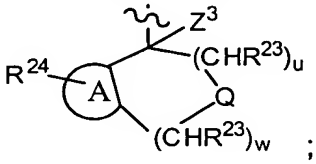



, and X^1 and X^2 together are

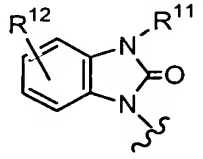


, R^{11} is not H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$hydroxyalkyl;

provided that when R^2 and R^4 form an alkylene bridge, Z^1, Z^2 and Z^3, together with the carbon to which they are attached, are not

; and



provided that when X^1 is and Z^1 is R^6-$(C_3\text{-}C_{12})$-cycloalkyl, Z^2 is not H; and

a therapeutically effective amount of a second agent selected from the group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, H_3 inhibitors, ß-adrenergic receptor agonists, xanthine derivatives, α–adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, NK_1, NK_2 and NK_3 tachykinin receptor antagonists, and $GABA_B$ agonists; and a pharmaceutically acceptable carrier.